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November 14, 2001

The Honorable Christine Todd Whitman
Administrator
U.S. Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on HPV Test Plan and Robust Summaries for Tall Oil and Related Substances

Dear Administrator Whitman:

The following comments on the test plan for "Tall Oil and Related Substances" are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than nine million Americans.

The Pine Chemicals Association, Inc.'s (PCA's) test plan for "Tall Oil and Related Substances" calls for an acute fish toxicity test, *in vitro* genotoxicity tests, and a combined repeat dose/repro/ developmental toxicity test (OECD TG 422). This test plan is yet another example of a proposal of irrelevant and inappropriate experiments. The plan violates the following terms of the October 1999 Agreement outlining principles to reduce repetitive or uninformative tests on animals:

1. In analyzing the adequacy of existing data, participants shall conduct a thoughtful, qualitative analysis rather than use a rote checklist approach. Participants may conclude that there is sufficient data, given the totality of what is known about a chemical, including human experience, that certain endpoints need not be tested.

2. Participants shall maximize the use of existing and scientifically adequate data to minimize further testing.

3. Participants shall maximize the use of scientifically appropriate categories of related chemicals and structure activity relationships.

8. In analyzing the adequacy of screening data for chemicals that are substances Generally Recognized as Safe (GRAS) for a particular use by the Food and Drug Administration (FDA), participants should consider all relevant and available information supporting the FDA's conclusions. Participants reviewing the adequacy of existing data for these chemicals should specifically consider whether the information available makes it unnecessary to proceed with further testing involving animals. As with all chemicals, before generating new information, participants should further consider whether any additional information obtained would be useful or relevant.

Our main objections to this test plan are as follows:

1. **The test plan does not reflect a thoughtful assessment of the value of additional tests in providing hazard information on the tall oil mixtures.**

2. **A large body of existing information is available to characterize the toxicity of the tall oil mixtures.**

3. **The test plan epitomizes the lack of inter-industry cooperation under the HPV program, resulting in redundant testing and unnecessary animal suffering.**

The Lack of Thoughtful Toxicology

The major components of the Tall Oil and Related Substances category include fatty acids, rosins, and sterols. The fatty acids are the main components of the mixtures and include palmitic acid, stearic acid, oleic acid, and linoleic acid.

Palmitic acid is the major fat in meat and dairy products. Oleic acid is the major fatty acid in olive oil and canola oil and is also a component of the fatty tissue of fish. Linoleic acid is an essential fatty acid and the major component of corn oil and soybean oil and is also a component of the fatty tissue of fish. Stearic acid is found in both animal and plant sources and is used as a flavoring agent. All of these chemicals are labeled "Generally Recognized as Safe (GRAS)" food additives by the Food and Drug Administration. Tall oil itself, the representative member of the category for which testing is proposed, is also labeled a GRAS food additive by the FDA.

Testing the tall oil mixtures on animals presents many challenges in the interpretation of experimental results. Over half of the mixture is made up of nutritional components. Among many other variables, the role of the diet can affect results. Exposure to the tall oil mixtures can change the caloric value and composition of saturated fats in the diet.

Testing the tall oil mixtures on fish is especially inappropriate because the insolubility of the fatty acids hinders the ability to conduct aquatic tests. The tall oil mixtures are characterized by a very low water solubility and they lack a functional group that would be susceptible to hydrolysis.

The PCA acknowledges the limitations of testing tall oil mixtures in aquatic environments and therefore proposes to manipulate experimental conditions to enhance solubility. The PCA does not describe how it intends to alter the OECD test guidelines, but does raise the possibility that the experimental conditions themselves "may cause non-specific toxicological effects." This confounds the experimental results and leads to difficulty in interpretation. The relevance of those experimental results for predicting aquatic toxicity of tall oil mixtures is highly questionable at best.

Without a detergent, the oil will just simply sit on top of the water and will not be bioavailable to the fish subjected to acute toxicity tests. A detergent could be added to enhance solubility, but detergents are associated with toxic effects. Sonic emulsification could also be used to increase water solubility. However, this leads to problems because the type and composition of droplets will affect the absorption of the substances. Steroid compounds could be embedded within the droplet and would be less likely to get absorbed.

Abundant Existing Information

There is ample human data on plant steroids, including studies on soy, phytoestrogens, and soy margarines.

As mentioned above, many of the specific compounds, as well as the complex mixture of tall oil to be tested are already listed as GRAS. The test plan presents no information on the basis for the GRAS listing and does not mention the information that was the basis of this decision. Ingestion of dietary phytosterols, which are components of the tall oil mixtures, has been shown to lower plasma lipid concentrations in humans and nonhuman animals. Many clinical studies on the medicinal effects of phytosterols have been conducted with human subjects.[1-6]

The effects of tall oil and its components, such as rosin (also called colophony), have been studied in different species, including humans. The main health concerns of exposure to these substances is allergic and sensitizing effects, such as contact dermatitis and occupational asthma.[7-14]

Lack of Inter-Industry Coordination

The main components of the tall oil mixtures, such as palmitic acid, stearic acid, oleic acid, and linoleic acid, are also found in another category proposed by the PCA, "Tall Oil Fatty Acids and Related Substances," posted on July 17, 1999. These two categories must be combined to reduce duplicative testing and maximize the use of structure activity relationships. A failure to do so is a clear violation of principle 3 of the October 1999 Agreement.

Moreover, palmitic acid, stearic acid, oleic acid, and linoleic acid are all being sponsored by the Soap and Detergent Association. Under the HPV framework and the October 1999 Agreement, these chemicals clearly should all be combined into one category. This test plan reflects a complete lack of inter-industry cooperation. The EPA must reject this test plan as scientifically unjustified and an inappropriate use of a large number of animals, and a clear violation of the October 1999 Agreement. We again reiterate our request to the EPA to inform us of how it intends to encourage better inter-industry collaboration and cooperation to eliminate repetitive tests.

Thank you for the opportunity to comment. I can be reached at 202-686-2210, ext. 302, or via e-mail at <ncardello@pcrm.org>. Correspondence should be sent to my attention at PCRM, 5100 Wisconsin Ave., N.W., Washington, DC 20016. I look forward to your response on these important issues.

Sincerely,

Nicole Cardello, M.H.S.
Staff Scientist

References

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